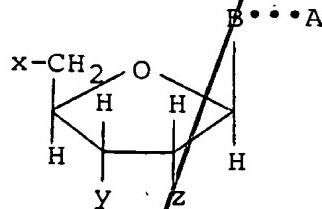


1. A compound having the structure:

5



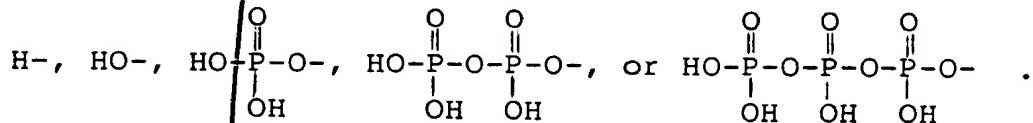
wherein B represents a purine, 7-deazapurine or pyrimidine moiety covalently bonded to the C<sup>1'</sup>-position of the sugar moiety, provided that when B is purine or 7-deazapurine, it is  
10 attached at the N<sup>9</sup>-position of the purine or deazapurine, and when B is pyrimidine, it is attached at the N<sup>1</sup>-position;

wherein A represents a moiety consisting of at least three carbon atoms which is capable of forming a detectable com-  
15 plex with a polypeptide when the compound is incorporated into a double-stranded ribonucleic acid, deoxyribonucleic acid duplex, or DNA-RNA hybrid;

wherein the dotted line represents a linkage or group joining B and A, provided that if B is purine, the linkage is attached to the 8-position of the purine, if B is 7-deaza-  
20 purine, the linkage is attached to the 7-position of the deazapurine, and if B is pyrimidine, the linkage is attached to the 5-position of the pyrimidine; and

25

wherein each of x, y and z represents



30

2. A compound in accordance with Claim 1 wherein B is uracil, cytosine, deazaadenine, or deazaguanine;

35 3. A compound in accordance with Claim 1 wherein A is a hapten.

4. A compound in accordance with Claim 1 wherein A is a ligand.

5. A compound in accordance with Claim 1 wherein A is biotin.

5

6. A compound in accordance with Claim 1 wherein A is iminobiotin.

7. A compound in accordance with Claim 1 wherein A is an  
10 organic moiety containing at least five carbon atoms.

8. A compound in accordance with Claim 1 wherein A is a non-aromatic organic moiety.

15 9. A compound in accordance with Claim 1 wherein the chemical linkage represented by the dotted line includes an olefinic bond at the  $\alpha$ -position relative to B.

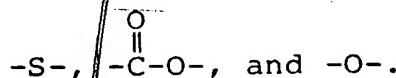
10. A compound in accordance with Claim 1 wherein the chemical linkage includes the moiety  $-\text{CH}_2\text{-NH-}$ .  
20

11. A compound in accordance with Claim 9 wherein the olefinic chemical linkage is  $-\text{CH=CH-CH}_2\text{-NH-}$ .

25 12. A compound in accordance with Claim 9 wherein the olefinic chemical linkage is  $-\text{CH=CH-CH}_2\text{-O-CH}_2\text{-CH(OH)-CH}_2\text{-NH-}$ .

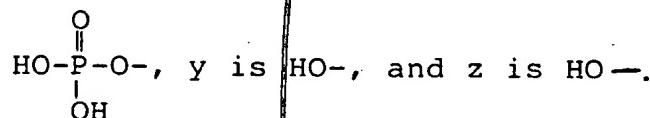
OH

13. A compound in accordance with Claim 1 wherein the chemical linkage is selected from or includes a moiety selected from the group consisting of

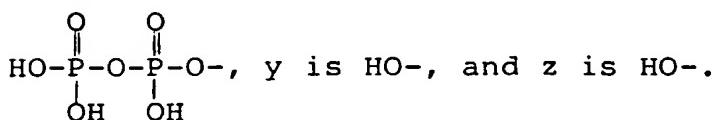


14. A compound in accordance with Claim 1 wherein x is

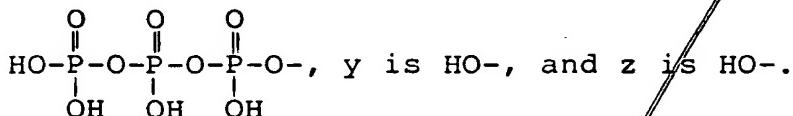
35



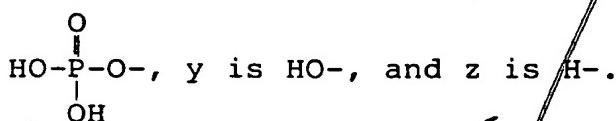
15. A compound in accordance with Claim 1 wherein x is



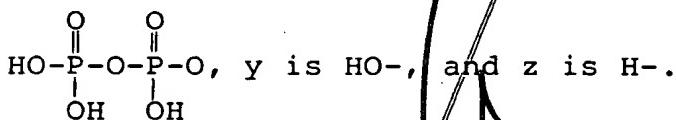
5 16. A compound in accordance with Claim 1 wherein x is



10 17. A compound in accordance with Claim 1 wherein x is



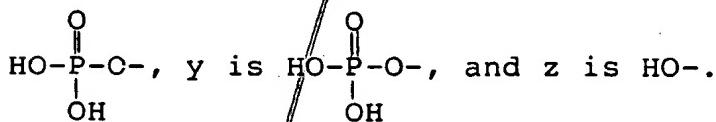
15 18. A compound in accordance with Claim 1 wherein x is



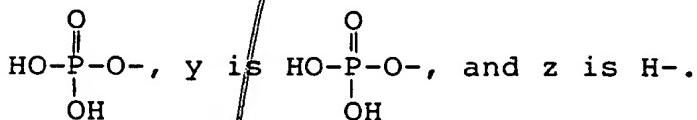
20 19. A compound in accordance with Claim 1 wherein x is



25 20. A compound in accordance with Claim 1 wherein x is



30 21. A compound in accordance with Claim 1 wherein x is



22. A compound in accordance with any of Claims 14, 15, 16, 17, 18, 19, 20, or 21 wherein A is biotin.

23. A compound in accordance with any of Claims 14, 15, 16, 17, 18, 19, 20, or 21 wherein A is iminobiotin.

5

24. A compound in accordance with any of Claims 14, 15, 16, 17, 18, 19, 20, 21, 22, or 23, wherein the chemical linkage is -CH=CH-CH<sub>2</sub>-NH-.

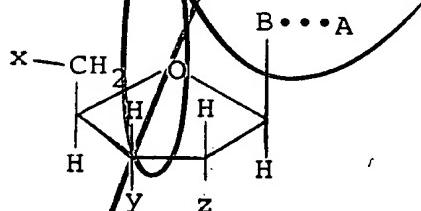
10 25. A compound in accordance with any of Claims 14, 15, 16,  
17, 18, 19, 20, 21, 22, or 23 wherein the chemical linkage  
is -CH=CH-CH<sub>2</sub>-O-CH<sub>2</sub>-CH-CH<sub>2</sub>-NH-.



15 26. A compound in accordance with any of Claims 14, 15, 16, 17,  
18, 19, 20, 21, 22, 23, 24, or 25 wherein B is uracil.

27. A method of preparing a modified nucleotide having the structure:

20



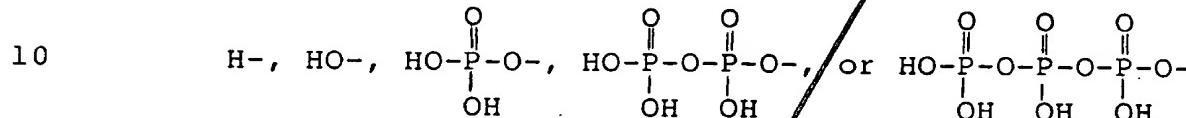
25 wherein B represents a purine, 7-deazapurine or pyrimidine moiety covalently bonded to the C<sup>1</sup>'-position of the sugar moiety, provided that when B is purine or 7-deazapurine, it is attached at the N<sup>9</sup>-position of the purine or deazapurine, and when B is pyrimidine, it is attached at the N<sup>1</sup>-position;

30

wherein A represents a moiety consisting of at least three carbon atoms which is capable of forming a detectable complex with a polypeptide when the compound is incorporated into a double-stranded ribonucleic acid, deoxyribonucleic acid duplex, DNA-RNA hybrid;

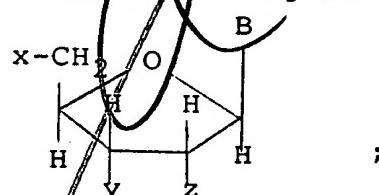
wherein the dotted line represents a chemical linkage joining B and A, provided that if B is purine, the linkage is attached to the 8-position of the purine, if B is 7-deaza-purine, the linkage is attached to the 7-position of the deazapurine, and if B is pyrimidine, the linkage is attached to the 5-position of the pyrimidine; and

wherein each of x, y, and z represents



comprising the steps of:

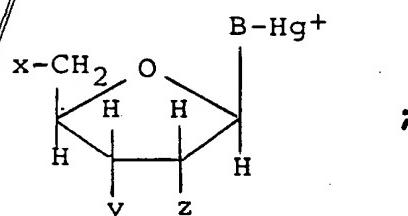
15      (a) reacting a compound having the structure:



20

with a mercuric salt in a suitable solvent under suitable conditions so as to form a mercurated compound having the structure:

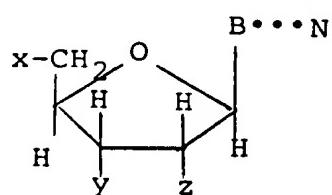
25



30

(b) reacting said mercurated compound with a chemical moiety reactive with the  $-\text{Hg}^+$  portion of said mercurated compound and represented by the formula  $\cdots \text{N}$ , said reaction being carried out in an aqueous solvent and in the presence of  $\text{K}_2\text{PdCl}_4$  under suitable conditions so as to form a compound having the structure:

35



wherein N is a reactive terminal functional group or  
is A; and

(c) recovering said compound as said modified nucleotide when N is A, or when N is a reactive terminal group, reacting said compound with a compound having the structure M-A, wherein M represents a functional group reactive with N in an aqueous solvent under suitable conditions so as to form said modified nucleotide, which is then recovered.

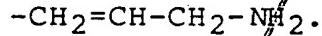
10

28. A method in accordance with Claim 27 wherein said suitable conditions comprise a pH in the range from about 1 to 14, a temperature in the range from about 5° to 100° C, and a reaction time in the range from about 3 to 24 hours.

15

29. A method in accordance with Claim 27 wherein said mercuric salt is mercuric acetate.

30. A method in accordance with Claim 27 wherein said chemical moiety represented by the formula •••N is



31. A method in accordance with Claim 27 wherein said chemical moiety represented by the formula •••N is

25           
$$-\text{CH}_2=\text{CH}-\text{CH}_2-\text{O}-\text{CH}_2-\underset{\text{OH}}{\text{CH}}-\text{CH}_2-\text{NH}_2.$$

32. A method in accordance with Claim 27 wherein said aqueous solvents include a buffer.

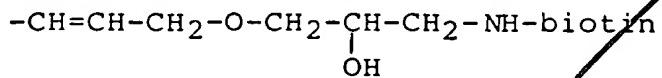
30

33. A method in accordance with Claim 32 wherein said buffer comprises sodium acetate, potassium acetate, sodium citrate, potassium citrate, potassium citrate-phosphate, tris-acetate, and borate-sodium hydroxide.

35

34. A method in accordance with Claim 33 wherein the concentration of said buffer is less than about 2.0 molar.
35. A method in accordance with Claim 27 wherein in step  
5 (b) the aqueous solvent additionally includes an organic solvent.
36. A method in accordance with Claim 35 wherein said organic solvent is water-miscible.  
10
37. A method in accordance with Claim 35 wherein said organic solvent comprises ethers, alcohols, esters, ketones, and amides.
- 15 38. A method in accordance with Claim 37 wherein said organic solvent comprises methanol, ethanol, propanol, glycerin, dioxane, acetone, pyridine, and dimethylformamide.
- 20 39. A method in accordance with Claim 27 wherein A comprises biotin or iminobiotin, and M comprises N-hydroxysuccinimide ester, imidate, anhydride, isothiocyanate, and epoxide.  
25
40. A method in accordance with Claim 27 wherein M is an N-hydroxysuccinimide ester.
41. A method in accordance with Claim 27 wherein M comprises imidate, anhydride, isothiocyanate, and epoxide.
- 30 42. A method in accordance with Claim 27 wherein •••N comprises thiol, carboxylic acid, epoxide, and amine.
43. A method in accordance with Claim 27 wherein said chemical moiety represented by the formula •••N is  
35            $-\text{CH}=\text{CH}-\text{CH}_2-\text{NH-}\text{biotin}.$

44. A method in accordance with Claim 27 wherein said chemical moiety represented by the formula  $\cdots \text{N}$  is

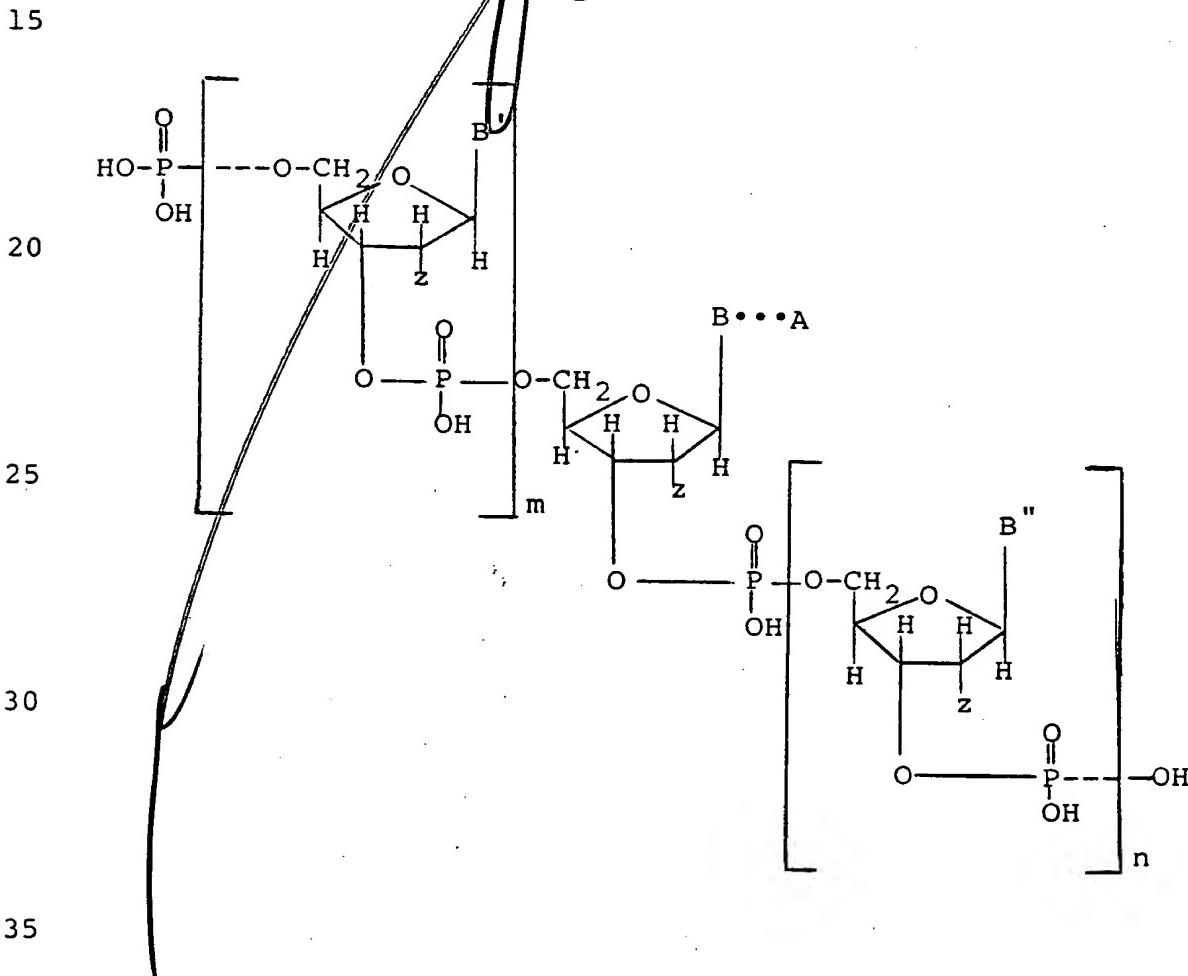


5 45. A method in accordance with Claim 27 wherein said  
chemical moiety represented by the formula \*\*\*N is  
-CH=CH-CH<sub>2</sub>-NH-iminobiotin.

46. A method in accordance with Claim 27 wherein said  
10 chemical moiety represented by the formula \*\*\*N is  
-CH=CH-CH<sub>2</sub>-O-CH<sub>2</sub>-CH=CH<sub>2</sub>-NH-iminobiotin.



47. A compound having the structure:



wherein each of B, B', and B" represents a purine, deaza-purine, or pyrimidine moiety covalently bonded to the C<sup>1'</sup>-position of the sugar moiety, provided that whenever B, B', or B" is purine or deaza-purine, it is attached at the N<sup>9</sup>-position of the purine or deaza-purine, and whenever B, B', or B" is pyrimidine, it is attached at the N<sup>1</sup>-position;

5 wherein A represents a moiety consisting of at least three carbon atoms which is capable of forming a detectable complex with a polypeptide when the compound is incorporated 10 into a double-stranded duplex formed with a complementary ribonucleic or deoxyribonucleic acid molecule.

15 wherein the dotted line represents a chemical linkage or group joining B and A, provided that if B is purine, the linkage is attached to the 8-position of the purine, if B is 7-deaza-purine, the linkage is attached to the 7-position of the deaza-purine, and if B is pyrimidine, the linkage is attached 20 to the 5-position of the pyrimidine;

20 wherein z represents H- or HO-; and

25 wherein m and n represent integers from 0 up to about 100,000.

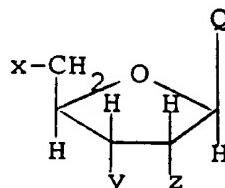
49. A compound in accordance with Claim 47 wherein m and n are not simultaneously 0.

30 50. A compound in accordance with Claim 47 wherein B is uracil, cytosine, deazaadenine, or deazaguanine.

35 51. A compound in accordance with Claim 47 wherein each B' and B" varies and is a uracil, cytosine, thymine, guanine, or adenine.

52. A compound in accordance with Claim 47 wherein A is a ligand.
- 5 53. A compound in accordance with Claim 52 wherein A is a hapten.
54. A compound in accordance with Claim 47 wherein A is biotin.
- 10 55. A compound in accordance with Claim 47 wherein A is iminobiotin.
- 15 56. A compound in accordance with Claim 47 wherein the chemical linkage represented by the dotted line includes an olefinic bond at the  $\alpha$ -position relative to B.
57. A compound in accordance with Claim 47 wherein the chemical linkage includes the moiety  $-\text{CH}_2\text{-NH-}$ .
- 20 58. A compound in accordance with Claim 56 wherein the olefinic chemical linkage is  $-\text{CH=CH-CH}_2\text{-NH-}$ .
- 25 59. A compound in accordance with Claim 56 wherein the olefinic chemical linkage is  $-\text{CH=CH-CH}_2\text{-O-CH}_2\text{-CH-CH}_2\text{-NH-}$ .  
OH
60. A compound in accordance with Claim 56 wherein the chemical linkage is selected from or includes a moiety selected from the group consisting of
- 30  $-\text{S}-$ ,  $-\text{C=O-}$ , and  $-\text{O-}$ .
61. A compound in accordance with Claim 47 wherein A is an organic moiety containing at least five carbon atoms.
- 35 62. A compound in accordance with Claim 47 wherein z is HO-
63. A compound in accordance with Claim 47 wherein z is H-.

64. A compound in accordance with Claim 62 or Claim 63 wherein A is biotin.
- 5 65. A compound in accordance with Claim 62 or Claim 63 wherein A is iminobiotin.
66. A compound in accordance with any of Claims 62, 63, 64, or 65 wherein the chemical linkage is  $-\text{CH}=\text{CH}-\text{CH}_2-\text{NH}-$ .
- 10 67. A compound in accordance with any of Claims 62, 63, 64, or 65 wherein the chemical linkage is  
 $-\text{CH}=\text{CH}-\text{CH}_2-\overset{\text{OH}}{\underset{\text{O}}{\text{C}}} \text{H}_2-\text{CH}-\text{CH}_2-\text{NH}-$ .
- 15 68. A compound in accordance with any of claims 62, 63, 64, 65, 66, or 67 wherein B is uracil.
69. A compound which comprises a plurality of structures in accordance with Claim 47 joined together.
- 20 70. A compound in accordance with Claim 69 wherein said plurality comprises from two up to about 30.
- 25 71. A method of making a compound in accordance with Claim 47 comprising an enzymatically polymerization of nucleotide triphosphates having the structure

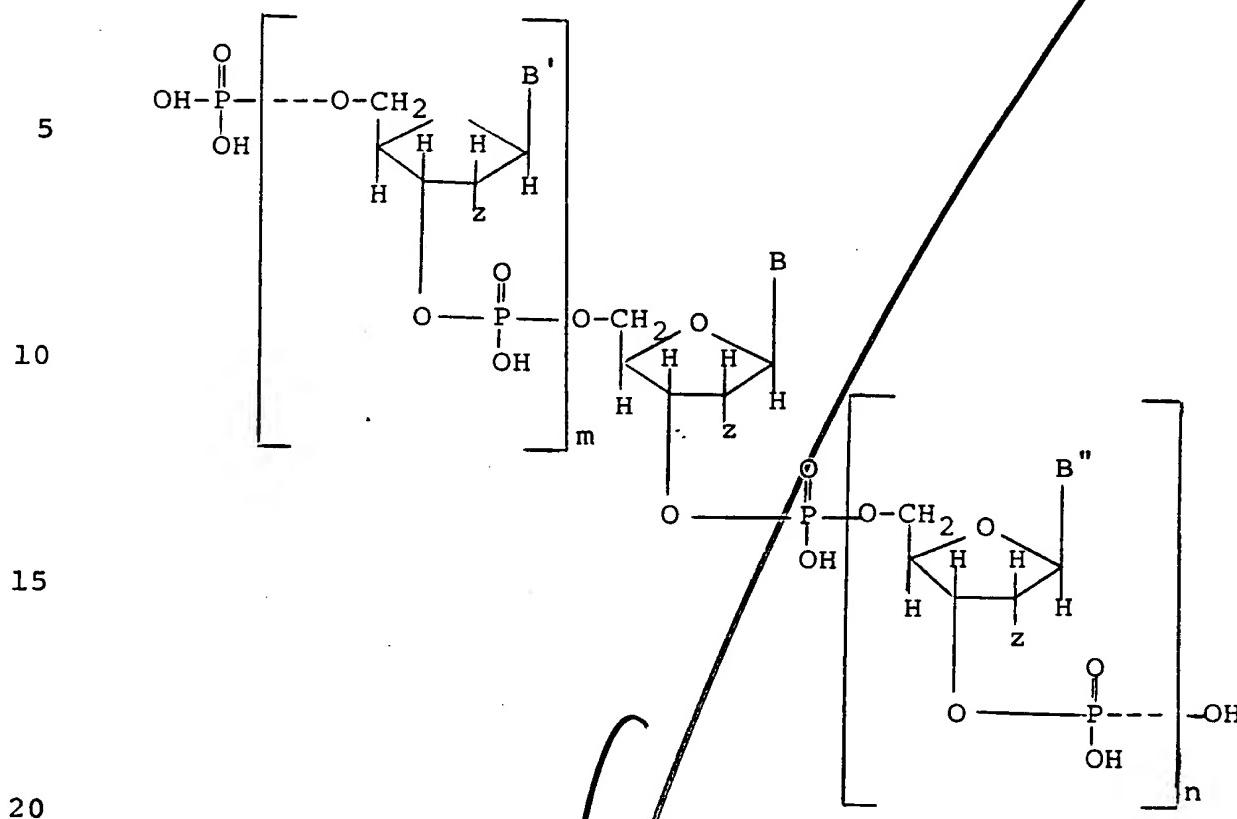


30 wherein Q represents  $\text{B}^{\bullet\bullet}\text{A}$ ,  $\text{B}'$ , or  $\text{B}''$ , and one of x and y represents  
 $\text{HO}-\overset{\text{O}}{\underset{\text{OH}}{\text{P}}}-\overset{\text{O}}{\underset{\text{OH}}{\text{P}}}-\overset{\text{O}}{\underset{\text{OH}}{\text{P}}}-\text{O}-$ , and the other of x and y  
35 represents  $\text{HO}^-$  in the presence of a nucleic acid

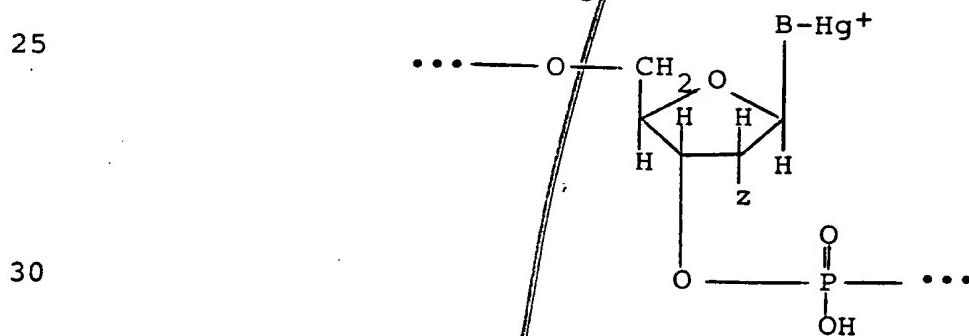
template under suitable conditions so as to form said compound.

- 5        72. A method in accordance with Claim 71 wherein said enzymatic polymerization comprises contacting said nucleotide triphosphates with a suitable enzyme selected from the group comprising DNA polymerase I of *E. coli*, bacteriophage T4 DNA polymerase, DNA polymerases  $\alpha$  and  $\beta$  from murine and human (HeLa) cells, DNA polymerase from Herpes simplex virus, RNA polymerase of *E. coli*, RNA polymerase of bacteriophage T7, eukaryotic RNA polymerase including HeLa cell RNA polymerase III, calf thymus RNA polymerase II, and mouse cell RNA polymerase II.
- 10      73. A method of making a compound in accordance with Claim 47 wherein n is 0 which comprises enzymatically adding a modified nucleotide in accordance with Claim 20 or Claim 21 to the end of an oligo- or polynucleotide under suitable conditions so as to form said compound.
- 15      74. A method in accordance with Claim 73 wherein said enzymatic addition comprises contacting said modified nucleotide with an RNA ligase.
- 20      75. A method of making a compound in accordance with Claim 47 comprising the steps of:

(a) reacting a compound having the structure:



with a mercuric salt in a suitable solvent under suitable conditions so as to form a mercurated derivative compound having the structure:

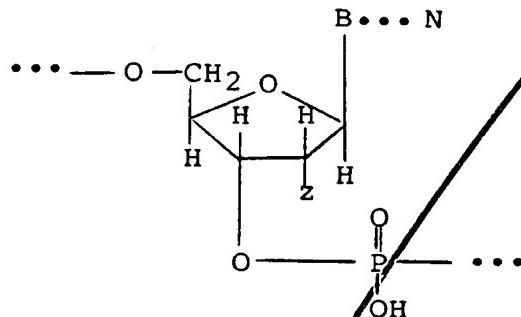


(b) reacting said mercurated derivative compound with a chemical moiety reactive with the  $-Hg^+$  portion of said mercurated compound and represented by the formula  $\cdots N$ , said reaction being carried out in an

aqueous solvent and in the presence of  $K_2PdCl_4$  under suitable conditions so as to form a compound having the structure:

5

10



wherein N is a reactive terminal functional group or is A; and

15

20

(c) recovering said compound of Claim 47 when N is A, or when N is a reactive terminal group, reacting said compound with a compound having the structure M-A wherein M represents a functional group reactive with N in an aqueous solvent under suitable conditions so as to form said compound of Claim 47, which is then recovered.

25

76. A method in accordance with Claim 75 wherein said suitable conditions comprise a pH in the range from about 1 to 14, a temperature in the range from about  $5^\circ$  to  $100^\circ$  C, and a reaction time in the range from about 3 to 24 hours.

30

77. A method in accordance with Claim 75 wherein said mercuric salt is mercuric acetate.

35

78. A method in accordance with Claim 75 wherein said chemical moiety represented by the formula  $\cdots N$  is  
 $-\text{CH}=\text{CH}-\text{CH}_2-\text{NH}_2$ .

35

79. A method in accordance with Claim 75 wherein said chemical moiety represented by the formula  $\cdots N$  is  
 $-\text{CH}=\text{CH}-\text{CH}_2-\text{O}-\text{CH}_2-\text{CH}-\text{CH}_2-\text{NH}_2$ .

OH

80. A method in accordance with Claim 75 wherein said aqueous solvents include a buffer.

5 81. A method in accordance with Claim 80 wherein said buffer comprises sodium acetate, potassium acetate, sodium citrate, potassium citrate, potassium citrate-phosphate, tris-acetate, and borate-sodium hydroxide.

10 82. A method in accordance with Claim 81 wherein the concentration of said buffer is less than about 2.0 molar.

15 83. A method in accordance with Claim 75 wherein in step (b) the aqueous solvent additionally includes an organic solvent.

84. A method in accordance with Claim 83 wherein said organic solvent is water-miscible.

20 85. A method in accordance with Claim 83 wherein said organic solvent comprises ethers, alcohols, esters, ketones, and amides.

25 86. A method in accordance with Claim 85 wherein said organic solvent comprises methanol, ethanol, propanol, glycerin, dioxane, acetone, pyridine, and dimethylformamide.

30 87. A method in accordance with Claim 85 wherein A comprises biotin or iminobiotin, and M comprises N-hydroxysuccinimide ester, imidate, anhydride, isothiocyanate and epoxide.

88. A method in accordance with Claim 75 wherein M is an N-hydroxysuccinimide ester.

35 89. A method in accordance with Claim 75 wherein M comprises imidate, anhydride, isothiocyanate, and epoxide.

90. A method in accordance with Claim 75 wherein  $\cdots N$  comprises thiol, carboxylic acid, epoxide, and amine.

5 91. A method in accordance with Claim 75 wherein said chemical moiety represented by the formula  $\cdots N$  is  
$$-\text{CH}=\text{CH}-\text{CH}_2-\text{NH}-\text{biotin}.$$

10 92. A method in accordance with Claim 75 wherein said chemical moiety represented by the formula  $\cdots N$  is  
$$-\text{CH}=\text{CH}-\text{CH}_2-\text{O}-\text{CH}_2-\underset{\text{OH}}{\text{CH}}-\text{CH}_2-\text{NH}-\text{biotin}.$$

15 93. A method in accordance with Claim 75 wherein said chemical moiety represented by the formula  $\cdots N$  is  
$$-\text{CH}=\text{CH}-\text{CH}_2-\text{NH}-\text{iminobiotin}.$$

20 94. A method in accordance with Claim 75 wherein said chemical moiety represented by the formula  $\cdots N$  is  
$$-\text{CH}=\text{CH}-\text{CH}_2-\text{O}-\text{CH}_2-\underset{\text{OH}}{\text{CH}}-\text{CH}_2-\text{NH}-\text{iminobiotin}.$$

25 95. A method of detecting a compound in accordance with Claim 1 which comprises contacting said compound with a polypeptide capable of forming a complex therewith under suitable conditions so as to form said complex, said polypeptide being capable of or including a moiety which can be detected when said complex of said compound and said polypeptide is formed, and detecting said complex using an appropriate detection technique.

30 96. A method in accordance with Claim 95 wherein the moiety A of said compound comprises biotin and iminobiotin.

35 97. A method in accordance with Claim 95 wherein said polypeptide comprises avidin, streptavidin, and IgG anti-A immunoglobulin.

98. A method in accordance with Claim 95 wherein the moiety A of said compound is a hapten and said polypeptide is an antibody.
- 5 99. A method in accordance with Claim 95 wherein the moiety A of said compound is a ligand.
100. A method in accordance with Claim 95 wherein the moiety included in said polypeptide which can be detected is a 10 fluorescent dye, electron dense reagent, or enzyme capable of depositing an insoluble reaction product.
- 10 101. A chemical complex comprising a compound in accordance with Claim 1 and a polypeptide capable of forming said complex with said compound.
- 15 102. A chemical complex in accordance with Claim 101 wherein said polypeptide includes a moiety which can be detected.
- 20 103. A chemical complex in accordance with Claim 102 wherein said detectable moiety is a fluorescent dye, electron dense reagent, or enzyme capable of depositing an insoluble reaction product.
- 25 104. A method of detecting a compound in accordance with Claim 47 which comprises contacting said compound with a polypeptide capable of forming a complex therewith under suitable conditions so as to form said complex, said polypeptide including a moiety which can be detected when said complex of said compound and said polypeptide is formed, and detecting said complex using an appropriate detection technique.
- 30 105. A method in accordance with Claim 104 wherein the moiety A of said compound comprises biotin and iminobiotin.
- 35

106. A method in accordance with Claim 104 wherein said polypeptide comprises avidin, streptavidin, and IgG anti-A immunoglobulin.

5 107. A method in accordance with Claim 104 wherein the moiety A of said compound is a hapten and said polypeptide is an antibody thereto.

108. A method in accordance with Claim 104 wherein the moiety A of said compound is a ligand.

10

109. A method in accordance with Claim 104 wherein the moiety included in said polypeptide which can be detected is a fluorescent dye, electron dense reagent, or enzyme capable of depositing an insoluble reaction product.

15

110. A chemical complex comprising a compound in accordance with Claim 47 and a polypeptide capable of forming said complex with said compound.

20

111. A chemical complex in accordance with Claim 110 wherein said polypeptide includes a moiety which can be detected.

25

112. A chemical complex in accordance with Claim 111 wherein said detectable moiety is a fluorescent dye, electron dense reagent, or enzyme capable of depositing an insoluble reaction product.

30

113. A method of detecting a double-stranded polynucleotide duplex which includes a compound in accordance with either <sup>Claim 125</sup> ~~either Claim 1 or Claim 47~~ which comprises contacting said polynucleotide duplex with a polypeptide capable of forming a complex therewith under suitable conditions so as to form said complex, said polypeptide including a moiety which can be detected when said complex of said polynucleotide duplex and said polypeptide is formed, and detecting said complex.

35

114. A method in accordance with Claim 113 wherein the moiety A of said polynucleotide duplex comprises biotin and iminobiotin.
- 5 115. A method in accordance with Claim 113 wherein said polypeptide comprises avidin, streptavidin, and IgG anti-A immunoglobulin.
- 10 116. A method in accordance with Claim 113 wherein the moiety A of said compound is a hapten and said polypeptide is an antibody thereto.
- 15 117. A method in accordance with Claim 113 wherein the moiety A of said compound is a ligand.
- 20 118. A method in accordance with Claim 113 wherein the moiety included in said polypeptide which can be detected is a fluorescent dye, electron dense reagent, or enzyme capable of depositing an insoluble reaction product.
- 25 119. A double-stranded polynucleotide duplex which includes a compound in accordance with either Claim 1 or Claim 47.
120. A duplex in accordance with Claim 119 wherein said polynucleotide strands are ribonucleic acid molecules.
- 25 121. A duplex in accordance with Claim 119 wherein said polynucleotide strands are deoxyribonucleic acid molecules.
- 30 122. A molecular complex comprising a duplex in accordance with Claim 119 and a polypeptide capable of forming said complex with said duplex.
- 35 123. A molecular complex in accordance with Claim 122 wherein said polypeptide includes a moiety which can be detected.

124. A molecular complex in accordance with Claim 123 wherein said detectable moiety is a fluorescent dye, electron dense reagent, or enzyme capable of depositing an insoluble reaction product.

5

125. A method of determining the presence of a deoxyribonucleic or ribonucleic acid molecule which comprises forming a double-stranded hybrid polynucleotide duplex which includes a single strand of deoxyribonucleic or ribonucleic acid corresponding to or derived from said deoxyribonucleic or ribonucleic acid molecule and a compound in accordance with Claim 47, and detecting said double-stranded hybrid polynucleotide duplex according to the method of Claim 113.

15

126. A method in accordance with Claim 125 wherein said deoxyribonucleic or ribonucleic acid molecule is derived from a living organism.

20

127. A method in accordance with Claim 125 wherein said living organism comprises bacteria, fungi, viruses, yeast, and mammals.

25

128. A method of diagnosing the presence of a nucleic acid-containing etiological agent in a subject which comprises obtaining a suitable sample from said subject, determining the presence in said sample of deoxyribonucleic or ribonucleic acid naturally associated with said etiological agent by forming a double-stranded polynucleotide duplex which includes a compound in accordance with Claim 47 and a single strand of deoxyribonucleic or ribonucleic acid corresponding to or derived from said deoxyribonucleic or ribonucleic acid which is naturally associated with said etiological agent under suitable conditions, and detecting the presence of said double-stranded polynucleotide duplex using the method of Claim 113.

35

129. A method in accordance with Claim 128 wherein said subject is human or animal and said etiological agent includes bacteria, viruses, and fungi.

5       130. A method of testing a bacterium to determine the presence of resistance to an antibiotic which comprises preparing a polynucleotide complementary to the deoxyribonucleic acid gene sequence of said bacterium which confers resistance to said antibiotic and includes the compound of  
10      Claim 1 incorporated therein, contacting said polynucleotide with deoxyribonucleic acid obtained from said bacterium under suitable conditions so as to form a double-stranded hybrid duplex, contacting said duplex with a polypeptide capable of forming a complex with said hybrid duplex under suitable  
15      conditions, said polypeptide including a moiety which can be detected if said complex is formed, and detecting the presence of said complex using an appropriate detection technique, the presence of said complex indicating resistance to said antibiotic and the absence of said complex indicating  
20      susceptibility to said antibiotic.

131.. A method in accordance with Claim 130 wherein said bacterium is Streptococcus pyogenes or Neisseria meningitidis and said antibiotic is penicillin.

25      132. A method in accordance with Claim 130 wherein said bacterium is Staphylococcus aureus, Candida albicans, Pseudomonas aeruginosa, Streptococcus pyogenes, or Neisseria gonorrhoeae and said antibiotic is a tetracycline.

30      133. A method in accordance with Claim 130 wherein said bacterium is Mycobacterium tuberculosis and said antibiotic is an aminoglycoside.

35      134. A method of diagnosing a genetic disorder in a subject which comprises preparing a polynucleotide complementary to

the deoxyribonucleic acid gene sequence of said subject which is associated with said genetic disorder and includes the compound of Claim 1 incorporated therein, contacting said polynucleotide with deoxyribonucleic acid obtained from 5 said subject under suitable conditions so as to form a double-stranded hybrid duplex, contacting said duplex with a polypeptide capable of forming a complex with said hybrid duplex, said polypeptide including a moiety which can be detected when said complex is formed, and detecting the presence of 10 said complex using an appropriate detection technique, the presence or absence of said complex indicating the presence or absence of said genetic disorder.

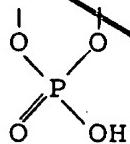
135. A method of diagnosing thalassemia in a human subject which comprises preparing a polynucleotide complementary to the deoxyribonucleic acid gene sequence which is absent in  $\beta$ -minus thalassemic subjects and includes the compound of Claim 1 incorporated therein, contacting said polynucleotide with deoxyribonucleic acid obtained from said subject 20 under suitable conditions so as to form a double-stranded hybrid duplex, contacting said duplex with a polypeptide capable of forming a complex with said hybrid duplex under suitable conditions, said polypeptide including a moiety which can be detected when said complex is formed, and 25 detecting the presence of said complex using an appropriate detection technique, the absence of said complex indicating the presence of  $\beta$ -minus thalassemia.

136. A method of chromosomal karyotyping which comprises 30 preparing a series of modified polynucleotides corresponding to a series of defined genetic sequences located on chromosomes, said polynucleotides including compounds in accordance with Claim 1, contacting said polynucleotides with deoxyriboxyribonucleic acid obtained from chromosomes so as 35 to form hybrid duplexes, contacting each of said duplexes with a polypeptide which is capable of forming a complex

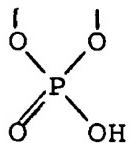
5 with each such duplex, said polypeptides including moieties which can be detected when said complexes are formed, and determining the location of each complex on said chromosomes so as to thereby determine the location of said genetic sequences on said chromosomes.

10 137. A method of detecting a polynucleotide which includes the terminal polynucleotide sequence poly A which comprises preparing a modified poly U molecule in which at least one uracil moiety has been modified by chemical addition at the 5-position of a moiety A consisting of at least three carbon atoms which is capable of forming a detectable complex with a polypeptide when the modified uracil moiety is incorporated into a double-stranded poly A-poly U duplex, forming such a poly A-poly U duplex by contacting said polynucleotide containing said poly A sequence with said modified poly U molecule under suitable conditions, and detecting resulting duplexes so as to thereby detect said polynucleotide.

15 20 138. A compound in accordance with Claim 1 in which z is H- or HO- and x and y are reacted to form the cyclic moiety



139. A compound in accordance with Claim 1 in which x is H- or HO- and y and z are reacted to form the cyclic moiety



35 140. A method of identifying hormone receptor sites on the surfaces of cells which comprises binding a compound in accordance with Claim 138 or 139 to the said sites under

*Sue  
B3*

suitable conditions permitting binding, disrupting said cells to produce cell surface fragments to which said compound is bound, separately recovering said cell surface fragment, and identifying the same so as to identify said hormone receptor sites.

141. A method of tumor or cancer cell identification which comprises detecting malignant cells by detecting abnormal hormonal receptor sites associated therewith according to the method of Claim 140.

142. A method of diagnosing a tumor cell which comprises preparing a polynucleotide which is complementary to a messenger ribonucleic acid synthesized from a deoxyribonucleic acid gene sequence associated with production of a polypeptide diagnostic for said tumor cell and includes a compound in accordance with Claim 1, introducing said polynucleotide into said cell under suitable conditions so as to permit said polynucleotide to hybridize with said deoxyribonucleic acid gene sequence, and determining whether said polynucleotide hybridizes.

143. A method in accordance with Claim 142 wherein said polypeptide is  $\alpha$ -fetal protein.

144. A method in accordance with Claim 142 wherein said polypeptide is carcinoembryonic antigen.

145. A diagnostic kit useful for determining the presence of a nucleic acid - containing organism such as a bacterium which comprises a compound in accordance with Claim 47 which is complementary to all or a unique portion of the nucleic acid contained in said organism and a polypeptide capable of forming a detectable complex therewith.

add  
C"

add  
53